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LETTERS AND CORRESPONDENCE

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Malignant Lymphoma in Association With Multiple Paraffin Implants

To the Editor: The safety of implantation of foreign material has been a subject of much discussion. There have been reports of connective tissue disease in women with augmentation mammoplasty. Silicone lymphadenopathy and malignant lymphoma have also been reported as an associated finding following mammoplasty [1,2] and arthroplasty [3–5].

In april 1996, a 65-year-old woman who was retired from movie acting had multiple cranial-nerve deficits and abdominal distension. She had diplopia at downward gaze, slow light reflexes of pupils, right-side (rt)-facial palsy, and ascites. In about 1960, paraffin materials were implanted in her breasts, shoulders, and wrists for cosmetic reasons. Results of blood values were as follows: hemoglobin level, 12.7 g/dl; leukocyte count, 11,000/μl (neutrophils, 69.3%; lymphocytes, 23.4%; monocytes, 5.7%; eosinophils, 0.7%; basophils 0.9%); and platelet count, 36.3×10^4/μl. The cerebrospinal fluid and peritoneal effusion contained large-cell lymphoma cells. The endoscopical examination of her stomach showed a submucosal tumor, the biopsy of which revealed non-Hodgkin's lymphoma (diffuse, large-cell type). Bone marrow aspiration was normal. She was admitted and treated with combined chemotherapy (vincristine, cyclophosphamide, prednisone, and THP-adriacin), resulting in partial remission. In December 1996, she had hypercalcemia and rt-intraorbital tumor and was treated with irradiation and combined chemotherapy; she then developed pneumonia and died of respiratory failure on March 4, 1997. Postmortem examination revealed a remission state of mmalignant lymphoma and pneumonia. Liquid paraffin material was found in her breasts, shoulders, and wrists in direct contact with the surrounding tissue. The microscopic description of pathology revealed exuberant granulomatous response with many vacuolated histiocytes (Fig. 1). Adjacent to some large vacuoles, there were intense infiltrates with lymphocytes and immunoblasts.

Our case report suggests that a possible association may exist between implants and malignant lymphoma. Lesions of malignant lymphoma appeared in the central nervous system, peritoneum, and stomach; therefore, they may not be related directly to the distribution of the implants. There have been a few reports of silicone lymphadenopathy with concomitant malignant lymphoma in cases with joint arthroplasty [3–5], follicular lymphoma adjacent to silicone breast prosthesis [2], and cutaneous T-cell lymphoma in association with silicone breast implants [1], and three of these cases had widespread lymphomas in bone marrow, skin, and lymph nodes distant from the implants. However, there is no report of liquid paraffin implants which may be different from silicone implants. The reason for the absence of the report is probably to be found in that the use of liquid paraffin in direct implants has been abandoned since about 1965 in Japan and other countries, and was replaced with the use of silicone compounds in bag implants. In contrast with bag implants, direct contact between paraffin implants and the surrounding tissues may cause a more severe type of immunological reaction. Hence, the wide distribution of implants and the possible migration of paraffin to distant sites may be related to the widespread development of malignant lymphoma associated with chronic foreign-body stimulation of the immune system.

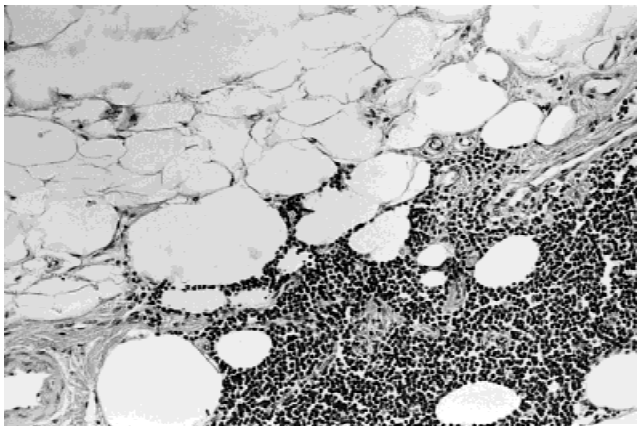

Fig. 1. Foreign body granulomatous reaction, typical of liquid forms of paraffin. Sections show many histiocytes filled with paraffin that resulted in intracytoplasmic vacuoles and imparted a foamy appearance. Some foreign-body giant cells are present. Adjacent to some large vacuoles, there were intense infiltrates with lymphocytes and immunoblasts.

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References

1. Duvic M, Moore D, Menter A, Vonderheid EC: Cutaneous T-cell lymphoma in association with silicone breast implants. J Am Acad Dermatol 32:939, 1995.
2. Cook PD, Osborne BM, Connor RL, Strauss JF: Follicular lymphoma adjacent to foreign body granulomatous inflammation and fibrosis surrounding silicone breast prothesis. Am J Surg Pathol 19:712, 1995.
3. Benjamin E, Ahmed A, Rashid ATMF, Wright DH: Silicone lymphadenopathy: A

report of two cases, one with concomitant malignant lymphoma. Diagn Histopathol 5:133, 1982.
4. Digby LM: Malignant lymphoma with intranodal silicone rubber particles following metacarpophalangeal joint replacements. Hand 14:326, 1982.
5. Murakata LA, Rangwala AF: Silicone lymphadenopathy with concomitant malignant lymphoma. J Rheumatol 16:1480, 1989.

Bone Marrow Mast Cell Disease Associated With Felty's Syndrome and Liver Cirrhosis

To the Editor: Disorders with mast cell proliferation, or so-called mastocytosis are rare [1]. Mastocytosis may be localized, limited to a single organ, or affect multiple organs such as skin, gastrointestinal tract, lymph nodes, liver, spleen, bone, and bone marrow [2], and histological diagnosis is necessary for confirmation [3]. Bone marrow mastocytosis is a prominent feature of primary mast cell disorders and has also been associated with a variety of hematologic and nonhematologic conditions such as chronic lymphoproliferative disorders, acute myeloid leukemia, aplastic anemia, bone marrow fibrosis, and osteoporosis [4]. In this report, we describe a rare case of mastocytosis in the bone marrow in a patient with Felty's syndrome and liver cirrhosis.

A 61-year-old woman was referred to our hospital because of pancytopenia. She had a 10-year history of seropositive rheumatoid arthritis that had been treated with intramuscular sodium aurothiomalate weekly and nonsteroidal antiinflammatory agents. Results of a general examination were unremarkable except for bilateral swollen knee joints with pain, and a nontender spleen that was palpable five cm below the costal margin. Laboratory data were as follows: hemoglobin concentration of 8.7 g/dl; a leukocyte count of 1.9×10^9/l with a differential of 46% neutrophils, 12% eosinophils, 34% lymphocytes; and a platelet count of 120×10^9/l. Aspartate aminotransferase and alanine aminotransferase were 34 international unit (IU)/l and 21 IU/l, respectively. Alkaline phosphatase was increased to 438 IU/l (normal range, 1–340). Serum rheumatoid factor was present at 86 IU/l (normal range, 0–20), but C-reactive protein level was under 0.5 mg/dl. Serum complement C3 and C4 levels were within normal limits and total protein level was 7.6 g/dl with an albumin of 3.8 g/dl. Hepatitis C virus antibody was positive. Bone marrow aspiration from the sternum showed a normal myeloid/erythroid ratio of 1.6:1. The differential count was 1.4% myeloblasts, 4.3% promyelocytes, 14.4% myelocytes, 7.2% metamyelocytes, 10.6% neutrophils, 10.4% eosinophils, 0.5% basophils, 3.4% monocytes, 13.6% lymphocytes, and a marked increase in the number of mast cells (0.6%) (Fig. 1). Abdominal computed tomography and ultrasonography revealed marked splenomegaly. She was subsequently diagnosed as having Felty's syndrome, and an elective splenectomy was performed. A 670 g spleen measuring $17 \times 15 \times 7$ cm was removed. The histological appearance of the excised spleen revealed reactive follicular hyperplasia of the white pulp in which dilatations of the sinus were detected. These findings were compatible with a diagnosis of Felty's syndrome. A liver biopsy was also performed during surgery that revealed cirrhosis with abundant micronodular pseudolobules. However, no evidence of mast cells was detected in either the spleen or liver. After splenectomy, the patient's hematologic abnormalities showed prompt improvement: a hemoglobin concentration of 10.2 g/dl, a leukocyte cell count of 8.3×10^9/l, and a platelet count of 446×10^9/l. However, bone marrow aspiration showed only a small decrease in the number of mast cells (0.4%).

Bone marrow mast cells were evident in this case, although she did not have any symptoms corresponding to mastocytosis in previous reports (pruritus, flushing, gastrointestinal symptoms) [1]. Mastocytosis without cutaneous manifestations are rare, accounting for approximately 1.0% of all cases [1]. Mastocytosis however, tends to mimic other disorders. Regarding the mechanism of mast cell proliferation in our case, both Felty's syndrome and liver cirrhosis may affect mast cell numbers in the bone marrow. Some reports have documented both intrahepatic mast cell infiltration in chronic liver disease [5], and splenomegaly with mast cell contents [2], although no mast cells were evident in the liver or spleen tissue specimens in our case. To our knowledge, there have been no previous reports of a correlation between mastocytosis and Felty's syndrome with liver cirrhosis. It remains unknown when mast cell proliferation occurred in the bone marrow. This is nevertheless a unique case presenting withmast cell proliferation in the bone marrow, in which the possible role of Felty's syndrome, or liver cirrhosis on mastocytosis, remains to be clarified.

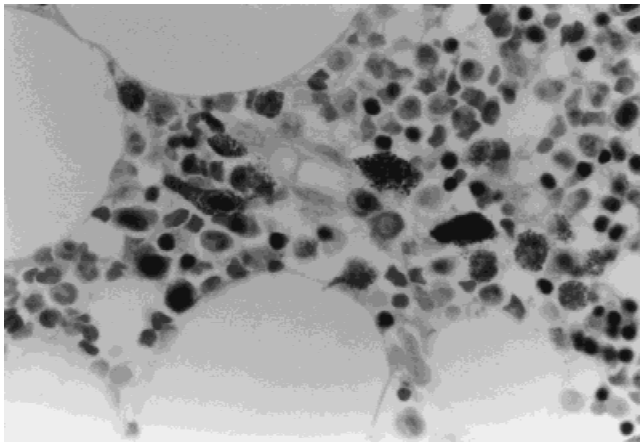

Fig. 1. Bone marrow aspiration showing an aggregation of mast cells (hematoxylin and eosin stain, ×200).

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References

1. Helen EB, Viraj S, Ligaya VC, Leonald B: Systemic mastocytosis: A diagnostic challenge. Ann Allergy 74:379–386, 1995.
2. Metcalfe DD: Mastocytosis. J Invest Dermatol 96:1S, 1991.
3. Travis WD, Li CY, Bergstralh EJ, Yam LT, Swee RG: Systemic mast disease. Analysis of 58 cases and literature review. Medicine 67:345, 1988.
4. Fohlmeister I, Reber T, Fischer R: Bone marrow mast cell reaction in preleukemia and aplastic anemia. Virchows Arch (A) 405:503, 1985.
5. Farrell DJ, Hines JE, Walls AF, Kelly PJ, Bennett MK, Burt AD: Intrahepatic mast cells in chronic liver diseases. Hepatology 22:1175, 1995.

Prothrombin Gene 20210 G-A Mutation in Turkish Patients With Thrombosis

To the Editor: Recent studies have demonstrated that common mutations in the genes encoding coagulation factor V (FV Leiden) and prothrombin